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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Yasmin Thanavala, et al.	Art Unit:	1651
Serial No:	09/420,695		
Filed:	October 19, 1999		
Examiner:	M. Flood		

I certify that this **APPEAL BRIEF** is being deposited on **April 2, 2001** with the U.S. Postal Service as first class mail addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231

Michael L. Dunn
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For: ORAL IMMUNOLOGY USING PLANT PRODUCT CONTAINING HEPATITIS SURFACE ANTIGEN

APPEAL BRIEF
(37 CFR 1.192)

Box AF
Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Applicants respectfully appeal the decision of the Examiner finally rejecting Claims 1 and 4-18 set forth in the Office Action dated October 4, 2000. A Notice of Appeal was timely filed by the Applicants on February 5, 2001 (mailed to the U.S.P.T.O. on Feb. 2, 2001).

Real Parties in Interest

The real parties in interest are Health Research, Inc. and Boyce Thompson Institute For Plant Research, Inc., assignees of the entire interest in the patent application.

Related Appeals and Interferences

There are no related appeals or interferences.

Status of Claims

The application originally contained 20 claims. Claims 2, 3, 19, and 20 have been cancelled. Claims 1, 4, 14 and 15 have been amended. Claims 1 and 4-18 are pending on Appeal.

Status of Amendments

Claims 1, 4, 14 and 15 have been amended. No amendments have been offered which have not been entered.

Summary of the Invention

The invention is a method for providing a serum IgM and IgG response to hepatitis B surface antigen (HBsAG), in an animal by feeding the animal with a substance comprising a physiologically acceptable plant material containing hepatitis B surface antigen in combination with an adjuvant. The combination causes serum IgM and IgG responses specific to HBsAg in excess of serum IgM and IgG responses specific to HBsAg caused by HBsAg alone.

The invention also includes the method as applied to humans and includes specific doses and procedures for that purpose.

Issues Presented for Review

Whether claims 1 and 4-18 are patentable under 35 USC 103 over U. S. Patent 5,935,570 to Arntzen et al. (B) in view of U.S. Patent 5,914,123 to Koprowski et al. (A), and further in view of Stites et al., Basic and Clinical Immunology, 7th ed., Appleton & Lange (U).

Grouping of Claims

The claims do not stand or fall together. It is not obvious from Claim 1 what methods, dosages and procedures would be suitable for obtaining a human immune response as set forth in subclaims.

Argument

The claims are unobvious to one skilled in the art and patentable over Arntzen et al. (B) in view of Koprowski et al. (A), and further in view of Stites et al. (U).

Arntzen et al. teaches a method for making a transgenic tobacco, tomato or potato that expresses HBsAg.

Notwithstanding the Examiner's assertion, **Arntzen et al. does not teach "methods of making a transgenic plant expressing an immunogen derived from hepatitis B surface antigen, wherein the immunogen is capable of eliciting an immune response in an animal by consumption of the plant material."**

Arntzen et al. pays lip service to raising an immune response by ingestion, but in fact give no examples or teachings for obtaining such a result. **The only actual plant examples in Arntzen et al. relate to tomatoes and tobacco. There is no example of ingestion of either one and certainly no example showing that ingestion of either raises an immune response.** In fact, ingestion of the transgenic tomato does not raise any significant immune response (see the enclosed Rule 132 Declaration of Dr. Yasmin Thanavala) and certainly tobacco cannot be used for such a purpose because it is toxic. **Since there is no teaching in Arntzen et al. of how oral immunization to HBsAg might be accomplished using a transgenic plant, and in fact**

the plants made in the examples do not function orally to raise an immune response, as Arntzen et al. alleges, it is clear that there is insufficient teaching or suggestion in Arntzen et al. to support a rejection of the present claims whether the reference is considered alone or in combination with the other cited references.

Simply making an unsupported allegation in a reference without a teaching as to how the allegation might be accomplished, is not a sufficient teaching to make a method for accomplishing the desired result obvious to one skilled in the art. Prophetic statements cannot be used to form the basis of a rejection, especially when they are unsupported and not true.

Arntzen et al. itself teaches and recognize that not all antigens would cause an immune response if ingested.

Arntzen et al. says in column 15 beginning at line 27,

"The vaccines are conventionally administered parenterally, by injection, for example either subcutaneously or intramuscularly. Additional formulations which are suitable for other modes of administration include suppositories and, ***in some cases***, oral formulations or aerosols." (emphasis added).

But there is no teaching or suggestion in Arntzen et al. of how the "some cases" could be determined or how the "some cases" could be accomplished.

While Arntzen et al. suggest that tomato juice containing HBsAg might be used as a vaccine, in fact Arntzen provides no supporting data showing any immune response whatsoever to tomato juice or any other plant containing HBsAg. To the extent that Arntzen teaches that tomato juice or any other plant material containing HBsAg can be used as a vaccine, it is an inoperative reference since there is no teaching or suggestion as to how that might be done.

Simply ingesting the plant material, as suggested by Arntzen et al., does not confer immunity at least in the sense that there is a protective response.

There is good reason for Arntzen's omission of data showing immune response to HBsAg by ingesting food material containing it, since prior to the present invention, in fact, there was little if any immune response whatsoever to HBsAg in orally ingested tomato juice or any other plant expressing HBsAg. **See the Rule 132 Declaration of Dr. Thanavala of record**. The response, if any, is clearly insufficient for that purpose.

Reference to the examples in the present specification clearly illustrates that priming of the subject of the immunization is required by either pre-vaccination or the use of an effective adjuvant. Arntzen et al. suggests neither. Arntzen et al. doesn't suggest an adjuvant for any purpose whatsoever and certainly does not suggest a combination with an adjuvant that permits the obtaining of a high immune response to orally administered HBsAg as required by the present claims.

Arntzen's suggestion of simple ingestion of plant material expressing HBsAg does not give a sufficient immune response to be considered protective. Arntzen discloses or suggests no way in which a high immune response could be orally obtained. ***In any case there is certainly no suggestion of the enhanced immune response to HBsAg in orally administered plant material as provided by the method presently claimed.***

The Examiner states that Koprowski "teaches methods of making a transgenic plant containing a viral antigen which is fed to an animal or human to elicit an immune response." The Examiner's statement is inaccurate. **Koprowski at al. does not teach or suggest any**

method for making a transgenic plant but teaches a microorganism expressing a bioactive compound, e.g. an immunogenic rabies polypeptide. The microorganism may then be used to infect a plant as a parasite but does not alter the genetic character or expression of the plant.

Koprowski et al. suggest that their method has wide application, e.g. for treatment of viral infections, bacterial infections, fungal infections, protozoan infections, diabetes, immune disorders, cancer and heart disease. Koprowski et al. more specifically suggest that their method could be used for mucosal pathogens, e.g. rabies, respiratory syncytial virus, cholera. typhoid fever, herpes simplex types I and II, tuberculosis, pathogenic pneumococci, human immunodeficiency virus-1 (HIV-1) and human immunodeficiency virus-2 (HIV-2).

The only specific example given is for rabies. There is no enablement for the other suggested applications. If the disclosure actually enabled everything suggested, oral vaccines effective against Aids, cancer, and herpes, among many others, would be made available simply by following the teachings of the Koprowski et al patent. It is well known that this is not the case.

Koprowski et al. certainly does not enable or even reasonably suggest application for orally raising an immune response to hepatitis B surface antigen. The suggestion that an adjuvant be used is a gratuitous statement applied across the entire non-enabled spectrum of the Koprowski et al. disclosure. There is no suggestion of any specific adjuvant that would have such an effect for purposes of enablement and in fact there is no suggestion that any adjuvant would have any effect whatsoever upon oral immune response to hepatitis B surface antigen and

certainly not with a genetically modified plant because Koprowski suggests nothing concerning a genetically modified plant.

Stites et al. adds nothing to cure the inadequate teachings and suggestions of Arntzen et al. and Koprowski et al. Stites does not suggest anything whatsoever concerning hepatitis B and certainly suggests nothing suggesting that HBsAg would or could **orally** raise a highly effective immune response in the presence of a suitable adjuvant as presently claimed. Adjuvants "enhance" immune response. Arntzen does not teach any method showing any immune response to be enhanced and especially not with respect to HBsAg.

In view of the foregoing amendments and remarks, it is courteously requested that all rejections be withdrawn and all claims be allowed.

Conclusion

In view of the foregoing, it is clear that the pending claims are patentable over the cited prior art. Reversal of the Examiner and allowance of all claims are therefore respectfully requested.

Respectfully submitted,

Dated: April 2, 2001

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Appendix

Reprinted below are the claims on appeal:

1. A method for providing a serum IgM and IgG response specific to hepatitis B surface antigen (HBsAG), in an animal by feeding the animal with a substance comprising a physiologically acceptable plant material containing hepatitis B surface antigen in combination with an adjuvant, said combination causing serum IgM and IgG responses specific to HBsAg in excess of serum IgM and IgG responses specific to HBsAg caused by HBsAg alone.

4. The method of claim 1 wherein the animal is a human.

5. The method of claim 4 wherein the plant material is from a plant that has been genetically altered to express said antigen.

6. The method of claim 5 wherein the human ingests sufficient plant material to provide from about 10 to about 100 micrograms of hepatitis B surface antigen per kilogram of body weight of the human.

7. The method of claim 6 wherein the human ingests sufficient plant material to provide from about 2 to about 5 grams of pant material per kilogram of body weight of the human.

8. The method of claim 5 wherein the human ingests said plant material a plurality of different times, said times being separated from each other by at least 5 days.

9. The method of claim 6 wherein the human ingests said plant material a plurality of different times, said times being separated from each other by at least 5 days.

10. The method of claim 7 wherein the human ingests said plant material a plurality of different times, said times being separated from each other by at least 5 days.

11. The method of claim 8 wherein the plurality of times is three times.

12. The method of claim 9 wherein the plurality of times is three times.

13. The method of claim 10 wherein the plurality of times is three times.

14. The method of claim 5 wherein the plant material is a material from a plant of the family *Solanaceae*.

15. The method of claim 6 wherein the plant material is a material from a plant of the family *Solanaceae*.

16. The method of claim 14 wherein the plant is a potato.

17. The method of claim 15 wherein the plant is a potato.

18. The method of claim 14 wherein the plant is a tomato.